UNIVERSITI PUTRA MALAYSIA

IMPACT OF GLUCOSE AND HIGH AFFINITY GLUCOSE SENSOR ON PHYSIOLOGICAL RESPONSES IN Candida glabrata

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FPSK(p) 2016 35

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By

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Thesis Submitted to the School of Graduate Studies, Universiti Putra Malaysia, in Fulfillment of the Requirements for the Degree of Doctor of Philosophy

October 2016

Abstract of thesis presented to the Senate of Universiti Putra Malaysia in fulfillment of the requirement of the degree of Doctor of Philosophy

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Chairman : Leslie Than Thian Lung, PhD
Faculty : Medicine and Health Sciences

Emerging fungal pathogen, *Candida glabrata* displays its metabolic flexibility by colonizing several site of host niches with different nutrient availability. Glucose sensing and utilization could be particularly important for the regulation of *C. glabrata* metabolic adaptation. Further exploration on the central metabolism pathway could help in advancing the knowledge on the novel antifungal development and overcome the limited choice of antifungal available currently. In line with this objective, the present study embarked on a several efforts in deciphering the role of glucose and glucose sensing in the viability and fitness of *C. glabrata*. The first part of this research outlined the putative genes of *C. glabrata* that are involved in the glucose inducing-Sugar Receptor-Repressor (SRR) pathway by comparing its orthologs found in *Saccharomyces cerevisiae*. Expression of selected key genes was also studied to confirm their response in five different glucose concentrations. For the second part, the phenotypic and physiological response of three strains of *C. glabrata* namely, ATCC2001 (laboratory isolate), Cg 2737 (clinical blood isolate) and Cg 91152 (clinical vaginal isolates), towards various glucose concentrations were studied. These strains were examined under different glucose concentration for their ability to grow, form biofilm, resistance toward amphotericin B (antifungal drug) and hydrogen peroxide (oxidative agent). Clinical isolates of *C. glabrata* were found with the ability to grow in low glucose environment (0.01%) where ATCC2001 strain has failed to survive. Generally, ATCC2001 and Cg 2737 was found to be active in biofilm formation under lower glucose environment (0.01, 0.1% and 0.2%) in comparison to glucose-rich environment (1% and 2%). Besides, low glucose surrounding (0.01, 0.1% and 0.2%) was also found to promote the survivability of *C. glabrata* towards amphotericin B (1 μg/ml), while higher glucose environment (0.2%, 1% and 2%) promotes *C. glabrata* resistance towards hydrogen peroxide. It is speculated that nutrient crisis in lower glucose setting is supposed to direct *C. glabrata* to a less active life cycle and therefore led it to group and form biofilm for nutrient sharing purposes. Lower metabolic rate and lower flux rate of molecules within *C. glabrata* biofilm may also result in the incompetence of

amphotericin B. Nevertheless, the promotion of anti H_2O_2 capability in *C. glabrata* by glucose requires further investigation. These observations have demonstrated the fine tuning of *C. glabrata* physiological behavior towards surrounding glucose levels as low as 0.01%. Besides, the higher expression of high affinity glucose sensor (*SNF3*) explained the ability of clinical isolates to grow in low glucose environment, in comparison to ATCC2001 strain. For the third part of this study, a *SNF3* knockout strain was constructed to study the role of this gene in the physiology of *C. glabrata*, particularly its involvement in the glucose sensing pathway. The *snf3*Δ showed a weaker growth of mutant strain under lower glucose environment (0.01% and 0.1%) in comparison to wild type. However, no different in growth was found when they were subjected to higher glucose concentration surrounding (1% and 2%). In addition, deletion of *SNF3* did not affect the ability of *C. glabrata* to form biofilm but instead disrupt the ability of *C. glabrata* to resist amphotericin B and survive in macrophage. Notably, deletion of *SNF3* resulted in the changes of transcription level for several key genes in the SRR pathway and suggested the shutting down of glucose uptake pathway that under low glucose environment. The disruption of *SNF3* was found to rattle the fitness of *C. glabrata*, particular in low glucose concentration environment, which is crucial for it to thrive in human niches site. This study has highlighted the impact of glucose on the physiology of *C. glabrata* and further decodes the involvement of *SNF3* in mediating the glucose uptake, which contributes to the vitality of *C. glabrata*.

Abstrak tesis yang dikemukakan kepada Senat Universiti Putra Malaysia sebagai memenuhi keperluan untuk ijazah Doktor Falsafah

KESAN GLUKOSA DAN PENDERIA GLUKOSA BERAFINITI TINGGI ATAS KE GERAK BALAS FISIOLOGI *Candida glabrata*

Oleh

NG TZU SHAN

Oktober 2016

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Sebagai patogen kulat yang baru muncul, *Candida glabrata* telah menunjukkan fleksibiliti metaboliknya dengan menjajah pelbagai lokasi dalam badan manusia yang mengandungi ketersediaan nutrien yang berbeza. Pencernaan dan penderiaan glukosa *C. glabrata* memainkan peranan penting dalam penyesuaian metaboliknya. Penyelidikan selanjut ke atas metabolisme berpusat dapat menyumbang dalam usaha menemui antikulat yang baru untuk menangani isu pilihan antikulat yang terhad. Selaras dengan objektif ini, beberapa usaha telah dijalankan untuk menerokai peranan glukosa dan penderiaan glukosa dalam pertumbuhan *C. glabrata*. Bahagian pertama kajian ini telah berjaya mengenal pasti gen-gen *C. glabrata* yang terlibat dalam proses Sugar Receptor-Repressor (SRR) dengan membandingkan ortholog mereka dalam *Saccharomyces cerevisiae*. Seterusnya, kajian ekspresi gen telah dijalankan untuk mengesah gerak balas gen-gen yang terpilih terhadap kepekatan glukosa yang berbeza. Untuk bahagian kedua, kajian gerak balas fenotip dan fisiologi bagi tiga isolat *C. glabrata*, iaitu ATCC2001 (isolat rujukan), Cg 2737 (isolat klinikal dari darah) dan Cg 91152 (isolat klinikal dari faraj) terhadap pelbagai kepekatan glukosa telah dijalankan. Dalam keadaan kepekatan glukosa yang berbeza, keupayaan ketiga-tiga *C. glabrata* ini dari segi pertumbuhan, pembentukan biofilm, rintangan terhadap amphotericin B (ubat antikulat) dan hidrogen peroksida (ejen oksidatif) telah dikaji. Isolat klinikal *C. glabrata* telah menunjukkan keupayaan mereka untuk bertumbuh dalam persekitaran yang mengandungi kepekatan glukosa yang rendah (0.01%), manakala ATCC2001 gagal bertumbuh dalam persekitaran yang sama. Secara umumnya, pembentukan biofilm oleh ATC2001 dan Cg 2737 adalah lebih aktif dalam persekitaran glukosa berkepekatan rendah (0.01%, 0.1% and 0.2%), jika dibandingkan dengan persekitaran glukosa berkepekatan tinggi (1% and 2%). Selain itu, persekitaran glukosa yang berkepekatan rendah (0.01%, 0.1% dan 0.2%) juga didapati dapat meningkatan rintangan *C. glabrata* terhadap amphotericin B (1 μg/mL). Sebaliknya, persekitaran glukosa berkepekatan tinggi (0.2%, 1% and 2%) dapat meningkatkan rintangan *C. glabrata* terhadap hidrogen peroxida. Krisis nutrien yang dihadapi oleh *C. glabrata* dalam persekitaran glukosa berkepekatan

rendah telah mengurangkan keaktifan cara hidup *C. glabrata*. Oleh itu, mereka terpaksa berkumpul dan hidup dalam biofilm demi perkongisian nutrien yang cekap. Sementara itu, kajian in mengspekulasi ketidakcekapan amphotericin B dalam kepekatan glukosa yang rendah adalah disebabkan oleh kadar metabolisma dan aliran molekul yang rendah dalam biofilm *C. glabrata*. Di samping itu, keupayaan tinggi *C. glabrata* terhadap antihidrogen peroksida dalam persekitaran glukosa berkepekatan tinggi adalah sesuatu yang tidak diketahui dan memerlukan penyelidikan selanjutnya. Data menunjukkan bahawa keupayaan *C. glabrata* dalam mengawal tingkah laku fisiologinya adalah bergantung kepada kandungan glukosa di persekitarannya. Selain itu, ekspresi gen penderia glukosa beraffiniti tinggi (*SNF3*) adalah lebih tinggi dalam isolat klinikal, berbanding dengan ATCC2001. Pemerhatian ini mungkin berkaitan dengan keupayaan isolat klinikal yang mampu bertumbuh dalam persekitaran glukosa berkepekatan rendah, berbanding dengan ATCC2001. Dalam bahagian ketiga kajian ini, mutan *C. glabrata* yang tanpa *SNF3* (*snf3*Δ) telah dihasilkan untuk mengkaji peranan *SNF3* dalam fisologi *C. glabrata*, terutamanya dalam proses penderiaan glukosa. Mutan *C. glabrata* telah menunjukkan kadar pertumbuhan yang lebih rendah dalam persekitaran glukosa berkepekatan rendah (0.01% dan 0.1%), berbanding dengan jenis liar. Walau bagaimanapun, kadar pertumbuhan dalam persekitaran glukosa berkepekatan tinggi (1% dan 2%) adalah sama bagi mutan dan jenis liar. Di samping itu, penyingkiran *SNF3* tidak menjejas keupayaan *C. glabrata* untuk membentuk biofilm. Di sebaliknya, ia menjejaskan keupayaan *C. glabrata* untuk menentang amphotericin B dan pertumbuhan *C. glabrata* di dalam makrofaj. Penyingkiran *SNF3* juga mengakibatkan perubahan transkripsi bagi beberapa gen dalam proses SRR dan dipercayai merencatkan proses pengangkutan glukosa ke dalam sel di persekitaran glukosa berkepekatan rendah. Data yang dikemukakan telah menunjukkan bahawa penyingkiran *SNF3* akan mengganggu pertumbuhan dan kercergasan *C. glabrata*, terutamanya dalam persekitaran glukosa berkepekatan rendah. Kajian ini telah memaparkan impak glukosa ke atas fisiologi *C. glabrata* dan peranan *SNF3* dalam mengkoordinasi pengambilan glukosa untuk pertumbuhan dan kercergasan *C. glabrata*.

ACKNOWLEDGEMENTS

First of all, I would like to thank my supervisor Dr. Leslie Than Thian Lung for his guidance, help, support and inspiration throughout the completion of this work. Thanks to Dr. Leslie for his effort and hard work in coordinating the Mycology Research Group to keep us together.

I also would like to express my gratitude to my supervisory committee members: Assoc. Prof. Dr. Mohd Nasir Mohd Desa, Dr. Doblin Sandai and Assoc. Prof. Dr. Chong Pei Pei for their constructive suggestion and criticism in my work.

I am also grateful to the financial support from MyBrain15 Scholarship, Ministry of Higher Education, Malaysia and RUGS Initiative 6, Universiti Putra Malaysia in making my study possible.

I also would like to thank to all the member of Biomedical Research lab, Mycology lab and Microbiology lab. Thanks to Shu Yih, Premmala, Kak Su, Eng Zhuan, Alan, Priya, Voon Kin, Kak Lina, Kak Fatimah, Kak Hanim, Kak Farah, En Zainal and En Yusop Radiman who helped me go through these few years in the lab.

I also want to thank my parents and family members for their continuous support and encouragement. I also would like to thank Ms Looi Ley Juen for her understanding, unwavering trust, and caring in supporting me throughout my study. Thank you for the endless love and support.

Finally, I would like to thank to everyone who I have met, either a blessing or a lesson. Thank you for being part of my life.

This thesis was submitted to the Senate of Universiti Putra Malaysia and has been accepted as fulfillment of the requirement for the degree of Doctor of Philosophy. The members of the Supervisory Committee were as follows:

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LIST OF ABBREVIATIONS

°C	Degrees Celsius
%	Percent
ABC	ATP-binding cassette
ATCC	American Type Culture Collection
ATP	Adenosine triphosphate
BLAST	Basic Local Alignment Search Tools
bp	Base pair
cAMP	Cyclic monophosphate
CDG	*Candida* Genome Database
cDNA	Complementary DNA
CFU	Colony forming unit
CHEF	Clamped homogenous electric field
CLSI	Clinical and Laboratory Standards Institute
CLSM	Confocal electron microscopy
CO_2	Carbon dioxide
DEPC	Diethyl pyrocarbonate
DMEM	Dulbecco's Modified Eagle's Medium
DMSO	Dimethyl sulfoxide
DNA	Deoxyribonucleic acid
dNTPs	Deoxynucleotide triphosphate
dsDNA	Double-stranded deoxyribonucleic acid
DTT	Dithiothreitol
EDTA	Ethylenediamine tetra acetic acid
EtBr	Ethidium bromide

FBS	Fetal bovine serum
FDA	Food and Drug Administration
g	Gram
GEXSR	Glucose-enhanced oxidative stress resistance
GOF	Gain of function
GPI	Glycosylphosphatidylinositol
h	Hour(s)
H_2O_2	Hydrogen peroxide
JTT	Jones-Taylor-Thornton
LiAc	Lithium acetate
M	Molar
MALDI-TOF	Matrix-assisted laser desorption ionization-time-of-flight
MEGA	Molecular Evolutionary Genetics Analysis
MFS	Major facilitator superfamily
MIC	Minimum inhibitory concentration
min	Minute
mL	Milliliter
MLST	Multilocus sequencing typing
mM	Milimolar
mRNA	Messenger RNA
NAD	Nicotinamide adenine dinucleotide
NADH	Nicotinamide adenine dinucleotide
NCAC	Non-Candida albicans Candida
NCBI	National Center for Biotechnology Information
NCCLS	National Committee for Clinical Laboratory Standards

ng	Nanogram
NJ	Neighbor Joining
nm	Nanometer
NRT	Non-reverse transcriptase
NTC	Non-template control
OD	Optical density
ORF	Open reading frame
PAGE	Polyacrylamide Gel Electrophoresis
PATH	Prospective Antifungal Therapy
PBS	Phosphate buffer saline
PCR	Polymerase chain reaction
PDREs	Pleiotropic drug response elements
PDS	Post-diauxic shift
PEG	Polyethylene glycol
PFGE	Pulsed-field gel electrophoresis
PKA	Protein kinase A
PPP	Pentose phosphate pathway
qRT-PCR	Quantitative real-time polymerase chain reaction
rDNA	Ribosomal deoxynucleic acid
rRNA	Ribosomal ribonucleic acid
REST	Relative Expression Software Tools
RNA	Ribonucleic acid
ROS	Reactive oxygen species
RPMI	Roswell Park Memorial Institute
rRNA	Ribosomal RNA

RT-PCR	Reverse transcriptase-polymerase chain reaction
SBP	Swi4-Swi6 cell cycle box binding factor
SC	Synthetic complete
SD	Synthetic defined minimal glucose media
sec	Second
SEM	Scanning electron microscopy
SEM	Standard error means
SRR	Sugar Receptor-Repressor
STRE	Stress-responsive element
TAE	Tris-acetate-EDTA
TBE	Tris-Boric acid-EDTA
TCA	Tricarboxylic acid
TE	Tris-EDTA
TES	Tris.Cl-EDTA-SDS
UMMC	University of Malaya Medical Center
UPM	Universiti Putra Malaysia
UV	Ultraviolet
V	Volt
w/v	Weight/Volume
WGD	Whole-genome duplication
XTT	2, 3-bis (2-methoxy-4-nitro-5-sulfophenyl)-2H-tetrazolium-5-carboxanilide
YPD	Yeast extract peptone dextrose
µg	Microgram
µL	Microlitre
µm	Micrometer

μM	Micromolar

GENE NOMENCLATURE

The nomenclature of *Candida* and *Saccharomyces cerevisiae* gene and protein are based on the Gene Nomenclature Guide, published in *Candida* Genome Database (www.candidagenome.org/Nomenclature. shtml) and also *Saccharomyces* Genome Database. An overview of the nomenclature guide is illustrated below:

Items	Descriptions	Example
Gene (loci)	Gene symbols comprise three italic letters (uppercase italic for dominant), and an Arabic number.	*ADE12*
Protein	Proteins are referred to by the relevant gene symbol, non-italic and initial letter uppercase.	Ade12

CHAPTER 1

INTRODUCTION

1.1 General introduction

The advancement of medicine such as organ transplant, medical devices implantation, wide distribution of corticosteroids and antimicrobial drugs does not only result in greater longevity of human but also cause the emergence of opportunistic fungal infections (Perfect & Casadevall, 2006; Collette & Lorenz, 2011). Of the 300,000 known fungal species, only a few fungi are capable of infecting human, including *Candida* species, *Aspergillus* species, *Cryptococcus neoformans*, *Histoplasma capsulatum* and so on (Ricardson, 1991; Perfect, 2016). Among these causative agents of fungal infections, *Candida* appears as the leading cause of opportunistic mycoses and also the fourth most common cause (accounted for 8% to 10%) of bloodstream infections acquired from hospital (nosocomial) in hospitalized patients (Wisplinghoff et al., 2004; Pfaller & Diekema, 2007; Perfect, 2016; Rajendran et al., 2016; Tan et al., 2016). A total of 72.8 - 290 cases of *Candida*-caused infection per million of population per year with high mortality rate (46% to 75%) were reported in United States (Eggimann et al., 2003; Wisplinghoff et al., 2004). Based on these statistics, the number of death due to nosocomial *Candida* bloodstream infection is estimated to be 2800 - 11200 death per year in United States (Pfaller & Diekema, 2007). On top of the high mortality rate, the prolonged hospitalization due to systemic invasive candidiasis has also resulted in costly medical fees, for example, a total of £16.2 million and $2 billion was estimated annually in managing candidiasis patients in the United Kingdom (except Scotland) and the United States, respectively (Wilson et al., 2002; Hassan et al., 2009).

Candidiasis may either be superficial, which involves the skin, hair, nails, oral and vaginal, or systemic, which affects the major body organs such as acute disseminated candidiasis (Molero et al., 1998; Fidel et al., 1999; Silva et al., 2011a). Recently, the incidence of candidiasis has continued to increase, particularly the systemic invasive candidiasis due to the exploited weakness in the human immune system. *Candida albicans*, *C. glabrata*, *C. parapsilosis* and *C. tropicalis* are among the dominant (>95%) causative agents for candidiasis (Pfaller & Diekema, 2010; Castanheira et al., 2016). Despite the dominance of *C. albicans* (> 50%), the noticeable emergence of non-*Candida albicans Candida* (NCAC) species, especially *C. glabrata* has also been reported in recent epidemiological reports studies (Pfaller et al., 2010; Diekema et al., 2012; Pfaller et al., 2014; Ng et al., 2015).

Glucose is known to be an important and precious source of nutrient for metabolism and growth of most living cells (Towle et al., 2005). The conserved glucose sensing and transportation found between prokaryote and eukaryote suggest the importance of these highly evolved and complete sensory mechanisms in the development of the organism, including pathogenic fungi (Sun et al., 2012). Adaptation through the

sensory mechanism is particularly important for pathogens in order to maintain its viability in various host niches and also to counteract the hostile environment such as microenvironment in phagocytes. In respect to the dynamic and complex environment in the host, the ability to respond to the constantly changing environmental nutrient availability is crucial for the survival of pathogen (Rodaki et al., 2009; Brown et al., 2014), e.g. the sudden nutritional starvation imposed on the phagocytes-trapped pathogen. Therefore, the ability to sense the surrounding nutrient, especially glucose is crucial in contributing to the growth and persistence of pathogen in the human host.

1.2 Problem statement

As an emerging and top two leading causative agent of candidiasis, the high mortality rate of *C. glabrata* fungemia has an important implications for therapy (Diekema et al., 2012). In comparison to antibacterial, there are only limited classes of antifungal agents available for physicians to combat this deadly fungal pathogen, namely polyenes, azoles, and echinocandins (Perfect, 2016). In addition to the innate resistance to azole drug group, the resistant to echinocandins observed in *C. glabrata* has complicated the management of patients (Pfaller et al., 2012). Taking antibacterial drug as an example, the worldwide explosion of antibacterial resistance has renewed the interest in the study of the central metabolism pathway, which has been known to be an unattractive drug target due to the lack of selectivity as most of the metabolic enzymes are conserved between bacteria and human (Murima et al., 2014). Similarly, most of the mainstream antifungals such as amphotericin B, fluconazole, and caspofungin target the cell wall and membrane of the fungal cell (Perfect, 2016). The interruption of cellular metabolism through the disrupted key nutrient sensory and transportation mechanisms, such as glucose sensing has been proved to affect the virulency of pathogenic fungi, *C. albicans* (Brown et al., 2006). Thus, it is essential to have a detailed study on this vital cellular process of the pathogenic fungi for the development of novel antifungal drug

The wide-ranged candidiasis suggests the incredible nutrient responsiveness of *Candida* species to thrive in diverging range of human anatomical site. Therefore, the ability to sense and utilize the glucose, particularly in the nutrient-limited niches is speculated to be important for the fitness of *Candida* species. Several studies have demonstrated the prominent effect of glucose availability in the physiological response and virulence traits of *C. albicans*, including the ability to form biofilm, resistance towards antifungals and oxidative stresses (Rodaki et al., 2009; Uppuluri et al., 2010). In addition, the reduced virulence of *C. albicans* and *Cryptococcus neoformans* in the disseminated murine model as a result of losing their high affinity glucose sensor suggest the vital role of this protein (Brown et al., 2006; Liu et al., 2013). However, little is known on the regulatory effect of glucose and the physiological role of high affinity glucose sensor in *C. glabrata*. Therefore, further investigation on these would serve as a continuous effort in the exploration of novel metabolic-targetted antifungal drug.

1.3 Objectives

In general, this study aimed to fill the gap of knowledge by revealing the regulatory effect of glucose and the importance of glucose sensing mechanism in the physiology of *C. glabrata*. The specific research objectives are as follows:

1. To identify and illustrate the glucose sensing and uptake pathway-related genes of *C. glabrata.*
2. To investigate the impact of glucose levels on *C. glabrata* viability and virulence.
3. To generate selected mutant strain for better understanding of the physiological role of selected genes in *C. glabrata.*

1.4 Thesis outline

This thesis is divided into six (6) chapters and formatted in accordance to the Style 2 as described in the Guideline to Thesis Preparation, Second Edition (June 2013), School of Graduate Studies, Universiti Putra Malaysia. Chapter 1 of this thesis portrays the brief introduction on candidiasis and *C. glabrata*, together with the needs and the objectives of this study. Chapter 2 is the literature review on the current knowledge of the biology of *C. glabrata* and the yeast glucose sensing/transportation mechanism as the subject of this study. Chapter 3 to Chapter 5 are the research chapters that discussed on three specific research objectives of this study. Chapter 6 is the general conclusion and recommendation that summarizes and concludes the findings of this study.

REFERENCES

Ahmad, K. M., Kokošar, J., Guo, X., Gu, Z., Ishchuk, O. P., & Piškur, J. (2014). Genome strauctures and dynamics of the yeast pathogen *Candida glabrata*. *FEMS Yeast Research*, 14, 529-35.

Ahmad, K.M., Ishchuk, O.P., Hellborg, L., Jørgensen, G., Skvarc, M., Stenderup, J., … Piškur, J. (2013). Small chromosomes among Danish *Candida glabrata* isolates originated through different mechanisms. *Antonie Van Leeuwenhoek*, 104, 111-122.

Alarco, A.M., & Raymond, M. (1999). The bZip transcription factor Cap1p is involved in multidrup resistance and oxidative stress response in *Candida albicans*. *Journal of Bacteriology*, 181, 700-708.

Alepuz, P.M., Cunningham., K.W., & Estruch, F. (1997). Glucose repression affects ion homeostasis in yeast through the regulation of the stress-activated *ENA1* gene. *Molecular Microbiology*, 26, 91-98.

Alonso-Monge, R., Navarro-Garcia, F., Román, E., Negredo, A.L., Eisman, B., Nombela, C., & Pia, J. (2003). The Hog1 mitogen-activated protein kinase is essential in the oxidative stress response and chlamydospore formation in *Candida albicans*. *Eukaryotic Cell*, 2, 351-361.

Alvarez, M., & Casadevall, A. (2006). Phagosome extrusion and host-cell survival after *Cryptococcus neoformans* phagocytosis by macrophages. *Current Biology*, 16, 2161-2165.

American Type Culture Collection. (2013). Product sheet of *Candida glabrata* (ATCC® 2001™). Retrieved from http://www.atcc.org/products/all/2001.aspx#characteristics.

Babu, P., Bryan, J.D., Panek, H.R., Jordan, S.L., Forrich, B.M., Kelley, S.C., … Robinson, L.C. (2002). Plasma membrane localization of the Yck2p yeast casein kinase 1 isoform requires the C-terminal extension and secretory pathway function. *Journal of Cell Science*, 115, 4957-4968.

Bader, O., Schwarz, A., Kraneveld, E.A., Tangwattanchuleeporn, M., Schmidt, P., Jacobsen, M.D., … Weig, M. (2012). Gross karyotypic and phenotypic alterations among different progenies of the *Candida glabrata* CBS138/ATCC2001 reference strain. *PLoS ONE*, 7, e52218.

Baillie, G.S., & Douglas, L.J. (1998). Effect of growth rate on resistance of *Candida albicans* biofilms to antifungal agents. *Antimicrobial Agents and Chemotherapy*, 42, 1900-1905.

Barelle, C.J., Priest, C.L., MacCallum, D.M., Gow, N.A., Odds, F.C., & Brown, A.J. (2006). Niche-specific regulation of central metabolic pathways in a fungal pathogen. *Cellular Microbiology*, 8, 961-971.

Barker, K.S., Crisp, S., Wiederhold, N., Lewis, R.E., Bareither, B., Eckstein, J., … Rogers, P.D. (2004). Genome-wide expression profilling reveals gene asscociated with amphotericin B and flucoanzole resistance in experimentally induced antifungal resistant isolates of *Candida albicans*. *The Journal of Antimicrobial Chemotherapy*, 54, 376-385.

Barns, S., Lane, D. J., Sogin, M. L., Bibeau, C., & Weisburg, W. (1991). Evolutionary relationships among pathogenic *Candida* species and relatives. *Journal of Bacteriology*, 173, 2250-2255.

Bassetti, M., Ansaldi, F., Nicolini, L., Malfatto, E., Molinari, M.P., Mussap, M., … Viscoli, C. (2009). Incidence of candidaemia and relationship with fluconazole use in an intensive care unit. *Journal of Antimicrobial Chemotherapy*, 64, 625-629.

Bennett, J.E., Izumikawa, K., & Marr, K.A. (2004). Mechanism of increased fluconazole resistance in *Candida glabrata* during prophylaxis. *Antimicrobial Agents and Chemotherapy*, 48, 1773-1777.

Berila, N., Borecka, S., Dzugasova, V., Bojnansky, J., & Subík, J. (2009). Mutations in the Cg*PDR1* and Cg*ERG11* genes in azole-resistant *Candida glabrata* clinical isolates from Slovakia. *International Journal of Antimicrobial Agents*, 33, 574-578.

Berman, J. (2016). Ploidy plasticity: A rapid and reversible strategy for adaptation to stress. *FEMS Yeast Research*, 16, pii: fow020.

Bialková, A., & Subík, J. (2006). Biology of the pathogen yeast *Candida glabrata*. *Folia Microbiologica*, 51, 3-20.

Bisson, L.F. (1988). High-affinity glucose transport in *Saccharomyces cerevisiae* is under general glucose repression control. *Journal of Bacteriology*, 170, 4838-4835.

Bisson, L.F., Coons, D.M., Kruckeberg, A.L., & Lewis, D.A. (1993). Yeast sugar transporters. *Critical Reviews in Biochemistry and Molecular Biology*, 28, 259-308.

Boles, E., & Hollenberg, C.P. (1997). The molecular genetics of hexose transport in yeasts. *FEMS Microbiology Reviews*, 21, 85-111.

Borst, A., Raimer, M.T., Warnock, D.W., Morrison, C.J., & Arthington-Skaggs, B.A. (2005). Rapid acquisition of stable azole resistance by *Candida glabrata* isolates obtained before the clinical introduction of fluconazole. *Antimicrobial Agents Chemotherapy*, 49, 783-787.

Brown, V., Sabina, J., & Johnston, M. (2009). Specialized sugar sensing in diverse fungi. *Current Biology*, 19, 436-441.

Brown, V., Sexton, J.A., & Johnston, M.A. (2006). A glucose sensor in *Candida albicans*. *Eukaryotic Cell*, 5, 1726-1737.

Brunke, S., & Hube, B. (2013). Two unlike cousins: *Candida albicans* and *C. glabrata* infection strategies. *Cell Microbiology*, 15, 701-708.

Buziol, S., Becker, J., Baumeister, A., Jung, S., Mauch, K., Reuss, M., & Boles, E. (2002). Determination of in vivo kinetics of the starvation-induced Hxt5 glucose transporter of *Saccharomyces cerevisiae*. *FEMS Yeast Research*, 2, 283-291.

Castanheira, M., Messer, S.A., Rhomberg, P.R., Pfaller, M.A. (2016). Antifungal susceptibility patterns of a global collection of fungal isolates: Results of the SENTRY Antifungal Surveillance Program (2013). *Diagnostic Microbiology and Infectious Disease*, 85, 200-204.

Castaño, I., Pan, S.J., Zupancic, M.L, Hennequin, C., Dujon, B., & Cormack, B.P. (2005). Telomere length control and transcriptional regulation of adhesins in *Candida glabrata*. *Molecular Microbiology*, 55, 1246-1258.

Chandra, J., Kuhn, D.M., Mukherjee, P.K., Hover, L.L., McCormick, T., & Ghannoum, M.A. (2001). Biofilm formation by the fungal pathogen *Candida albicans*: development, architecture, and drug resistance. *Journal of Bacteriology*, 183, 5385-5394.

Charlier, C., Hart, E., Lefort, A., Ribaud, P., Dromer, F., Denning, D.W., & Lortholary, O. (2006). Fluconazole for the management of invasive candidiasis: where do we stand after 15 years? *Journal of Antimicrobial and Chemotherapy*, 57, 384-410.

Chen, A., & Sobel, J. D. (2005). Emerging azole antifungals. *Expert Opinion on Emerging Drugs*, 10, 21-33.

Coco, B.J., Bagg, J., Cross, L.J., Jose, A., Cross, J., & Ramage, G. (2008). Mixed *Candida albicans* and *Candida glabrata* populations associated with the pathogenesis of denture stomatitis. *Oral Microbiology Immunology*, 23, 377-383.

Collart, M.A., & Oliviero, S. Preparation of yeast RNA. *Current Protocols in Molceular Biology*. 23, 13.12.1-13.12.5.

Collette, J.R., & Lorenz, M.C. (2011). Mechanism of immune evasion in fungal pathogens. *Current Opinion in Microbiology*, 14, 668-675.

Collette, J.R., Zhou, H., & Lorenz, M.C. (2014). *Candida albicans* suppresses nitric oxide generation from macrophage via secreted molecule. *PLoS ONE*, 9, e96203.

Colombo, A.L., Garnica, M., Aranha Camargo, L.F., Da Cunha, C.A., Bandeira, A.C., Borghi, D., … Nucci, M. (2013). *Candida glabrata*: an emerging pathogen in Brazilian tertiary care hospitals. *Medical Mycology*, 51, 38-44.

Compagno, C., Dashko, S., & Piškur, J. (2014). Introduction to carbon metabolism in yeast. In J, Piškur & C. Compagno (Eds.), *Molecular Mechanisms in Yeast Carbon Metabolism* (pp 1-20). Heidelberg: Spinger-Verlag.

Cormack, B.P., & Falkow, S. (1999). Efficient homologous and illegitimate recombination in the opportunistic yeast pathogen *Candida glabrata*. *Genetics*, 151, 979-987.

Cormack, B.P., Ghori, N., & Falkow, S. (1999). An adhesin of the yeast pathogen *Candida glabrata* mediating adherence to human epithelial cells. *Science*, 285, 578-582.

Costerton, J.W., Stewart, P.S., & Greenberg, E.P. (1999). Bacterial biofilms: a common cause of persistent infections. *Science*, 284, 1318-1322.

Cota, J.M., Grabinski, J.L., Talbert, R.L., Burgess, D.S., Rogers, P.D., Edlind, T.D., & Wiederhold, N.P. (2008). Increases in *SLT2* expression and chitin content are associated with incomplete killing of *Candida glabrata* by caspofungin. *Antimicrobial Agents and Chemotherapy*, 52, 1144-1146.

Csank, C & Haynes, K. *Candida glabrata* displays pseudohyphal growth. *FEMS Microbiology Letters*, 189, 115-120.

Cuéllar-Cruz, M., Briones-Martin-del-Campo, M., Cañas-Villamar, I., Montalvo-Arredondo, J., Riego-Ruiz, L., Castaño, I., De Las Peñas, A. (2008). High resistance to oxidative stress in the fungal pathogen *Candida glabrata* is mediated by a single catalase Cta1p, and is controlled by the transcription factors Yap1p, Skn7p, Msn2p, and Msn4p. *Eukaryotic Cell*, 7, 814-825.

De Deken, R.H. (1966). The Crabtree effect: a regulatory system in yeast. *Journal of General Microbiology*, 44, 149-156.

De Wet, N., Llanos-Cuentas, A., Suleiman, J., Baraldi, E., Krantz, E.F., Della Negra, M., & Diekmann-Berndt, H. (2004). A randomized, double-blind, parallel-group, dose-response study of micafungin compared with fluconazole for the treatment of esophageal candidiasis in HIV-positive patients. *Clinical Infectious Diseases*, 39, 842-849.

Deshaies, R. (1999). SCF and cullin/ring H2-based ubiquitin ligases. *Annual Review of the Cell and Development Biology*, 15, 435-467.

Diderich, J.A., Schepper, M., van Hoek, P., Luttik, M.A., van Dijken, J.P., Pronk, J.T., & Kruckeberg, A.L. (1999). Glucose uptake kinetics and transcription of *HXT* genes in chemostat cultures of *Saccharomyces cerevisiae*. *The Journal of Biological Chemistry*, 274, 15350-15359.

Diekema, D., Arbefeville, S., Boyken, L., Kroeger, J., & Pfaller, M. (2012). The changing epidemiology of healthcare-associated candidemia over three decades. *Diagnostic Microbiology and Infectious Diseases*, 73, 45-48.

Dietvorst, J., Karhumaa, K., Kielland-Brandt, M.C., & Brandt, A. (2010). Amino acid residues involved in ligand preference of the Snf3 transporter-like sensor in *Saccharomyces cerevisiae*. *Yeast*, 27, 131-138.

Dlugai, S., Hippler, S., Wieczorke, R., & Boles, E. (2001). Glucose-dependent and –independent signalling functions of the yeast glucose sensor Snf3. *FEBS Letters*, 505, 389-392.

Domergue, R., Castaño, I., De Las Peñas, A., Zupancic, M., Lockateli, V., Hebel, J.R., & Cormack, B.P. (2005). Nicotinic acid limitation regulates silencing of *Candida* adhesin during UTI. *Science*, 308, 866-870.

Douglas, L.J. (2003). *Candida* biofilms and their role in infection. *Trends in Microbiology*, 11, 30-36.

Dujon, B., Sherman, D., Fischer, G., Durrens, P., Casaregola, S., Lafontaine, I., … Souciet, J.L. (2004). Genome evolution in yeasts. *Nature*, 430, 35-44.

Dupont, B. (2002). Overview of the lipid formulations of amphotericin B. *The Journal of Antimicrobial Chemotherapy*, 49, 31-36.

Ehrström, S., Yu, A., & Rylander, E. (2006). Glucose in vaginal secretions before and after oral glucose tolerance testing in women recurrent vulvovaginal candidiasis. *Obstetrics and Gynecology*, 108, 1432-1437.

Ene, I.V., Adya, A.K., Wehmeier, S., Brand, A.C., MacCallum, D.M., Gow, N.A., Brown, A.J. (2012a). Host carbon source modulate cell wall architecture, drug resistance and virulence in a fungal pathogen. *Cellular Microbiology*, 14, 1319-1335.

Ene, I.V., Cheng, S.C., Netea, M.G., & Brown, A.J. (2013). Growth of *Candida albicans* cells on the physiologically relevant carbon source lactate affects their recognition and phagocytosis by immune cells. *Infection and Immunity*, 81, 238-248.

Ene, I.V., Heilmann, C.J., Sorgo, A.G., Walker, L.A., de Koster, C.G., Munro, C.A., & Brown, A.J. (2012b). Carbon source-induced reprogramming of the cell wall proteome and secretome modulating the adherence and drug resistance of the fungal pathogen *Candida albicans*. *Proteomics*, 12, 3164-3179.

Fan, J., Chaturvedi, V., & Shen, S.H. (2002). Identification and phylogenetic analysis of a glucose transporter gene family from the human pathogenic yeast *Candida albicans*. *Journal of Molecular Evolution*, 55, 336-346.

Felsenstein, J. (1985). Confidence limits on phylogenies: an approach using the bootstrap. *Evolution*, 39, 783.

Fernández-Arenas, E., Bleck, C.K., Nombela, C., Gil, C., Griffiths, G., Diez-Orejas, R. (2009). *Candida albicans* actively modulates intracellular membrane trafficking in mouse macrophage phagosomes. *Cellular Microbiology*, 11, 560-589.

Ferrari, S., Ischer, F., Calabrese, D., Posteraro, B., Sanguinetti, M., Fadda, G., & Sanglard, D. (2009). Gain of function mutations in Cg*PDR1* of *Candida glabrata* not only mediate antifungal resistance but also enhance virulence. *PLoS Pathogens*, 5, e1000268.

Fidel, P. Jr., Vazquez, J. A. & Sobel, J. D. (2011) *Candida glabrata*: an important fungal pathogen in 21st century. *Clinical Microbiology Newsletter*, 23, 171-176.

Fleck, C.B., Schöbel, F., & Brock, M. (2011). Nutrient acquisition by pathogenic fungi: nutrient availability, pathway regulation, and differences in substrate utilization. *International Journal of Medical Microbiology*, 301, 400-407.

Flick, K.M., Spielewoy, N., Kalashnikova, T.I., Guaderrama, M., Zhu, Q., Chang, H.C., Wittenberg, C. (2003). Grr1-dependent inactivation of Mth1 mediates glucose-induced dissociation of Rgt1 from *HXT* genes promoters. *Molecular Biology of the Cell*, 14, 3230-3241.

Flores, C.L., Rodriguez, C., Petit, T., & Gancedo, C. (2000). Carbonhydrate and energy-yielding metabolism in non-conventional yeast. *FEMS Microbiology Reviews*, 24, 507-529.

Fox, A. (2006). Mass spectrometry for species or strin identification after culture or without culture: Past, present, and future. *Journal of Clinical Microbiology*, 44, 2677-2680.

Fujita, S., Senda, Y., Nakaguchi, S., & Hashimoto, T. (2001). Multuplex PCR using internal transcribed spacer 1 and 2 regoins for rapid detection and identification of yeast strains. *Journal of Clinical Microbiology*, 39, 3617-3622.

Gabaldón T., Martin, T., Marcet-Houben, M., Durrens, P., Bolotin-Fukuhara, M., Lespinet, O., … Fairhead, C. (2013). Comparative genomics of emerging pathogens in the *Candida glabrata* clade. *BMC Genomics*, 14, 623.

Gallis, H.A., Drew, R.H., & Pickard, W.W. (1990). Amphotericin B: 30 years of clinical experience. *Reviews of Infectious Diseases*, 12, 308-329.

Gancedo, J.M. (1998). Yeast carbon catabolite repression. *Microbiology and Molecular Biology Reviews*, 62, 334-361.

Gancedo, J.M. (2008). The early steps of glucose signalling in yeast. *FEMS Microbiology Reviews*, 32, 673-704.

Goujon, M., McWilliam, H., Li, W., Valentin, F., Squizzato, S., Paern, J., & Lopez, R. (2010). A new bioinformatics analysis tools framework at EMBL-EBI. *Nucleic Acids Research*, 38, W695-W699.

Görner, W., Durchschlag, E., Martinez-Pastor, M.T., Estruch, F., Ammerer, G., Hamilton, B., … Schüller, C. (1998). Nuclear localization of the C2H2 zinc finger protein Msn2p is regulated by stress and protein kinase A activity. *Genes Development*, 12, 586-597.

Görner, W., Durchschlag, E., Wolf, J., Brown, E.L., Ammerer, G., Ruis, H., Schüller, C. (2002). Acute glucose starvation activates the nuclear location signal of a stress-specific yeast transcription factor. *The EMBO Journal*, 21, 135-144.

Grandin, N., Damon, C., & Charbonneau, M. (2001). Ten1 functions in telomere end protection and length regulation in association with Stn1 and Cdc13. *The EMBO Journal*, 20, 1173-1183.

Hardy, C.F., Sussel, L., & Shore, D. (1992). A *RAP1*- interacting protein involved in transcriptional silencing and telomere length regulation. *Genes & Development*, 6, 801-814.

Haro, R., Garciadeblas, B., & Rodriguez-Navarro, A. (1991). A novel P-type ATPas from yeast involved in sodium transport. *FEBS Letters*, 291, 189-191.

Hasan, F., Xess, I., Wang, X., Jain, N., & Fries, B.C. (2009). Biofilm formation in clinical *Candida* isolates and its association with virulence. *Microbes and Infection*, 11, 753-761.

Hassan, I., Powell, G., Sidhu, M., Hart, W.M., & Denning, D.W. (2009). Excess mortality, length of stay and cost attributable to candidaemia. *The Journal of Infections*, 59, 360-365.

Hawser, S.P., & Douglas, L.J. (1994). Biofilm formation by *Candida* species on the surface of catheter materials *in vitro*. *Infection and Immunity*, 62, 915-921.

Hedbacker, K., & Carlson, M. (2008). *SNF1*/AMPK pathway in yeast. *Frontiers in Bioscience*, 13, 2408-2420.

Hirayama, T., Maeda, T., Saito, H., & Shinozaki, K. (1995). Cloning and characterization of seven cDNAs for hyperosmolarity-responsive (HOR) genes of *Saccharomyces cerevisiae*. *Molecular & General Genetics*, 249, 127-138.

Hoffman, C.S. (1997). Preparation of yeast DNA. *Current Protocols in Molecular Biology*, 39, 13.11.1-13.11.4

Horák, J. (2013). Regulations of sugar transporters: insights from yeast. *Current Genetics*, 59, 1-31.

Hsiung, Y.G., Chang, H.C., Pellequer, J.L., La Valle, R., Lanker, S., & Wittenberg, C. (2001). F-box protein Grr1 interacts with phosphorylated targets via the cationic surface of its leucine-rich repeat. *Molecular and Cellular Biology*, 21, 2506-2520.

Hubbard, E.J., Jiang, R., & Carlson, M. (1994). Dosage-dependent modulation of glucose repression by *MSN3* (*STD1*) in *Saccharomyces cerevisiae*. *Molecular and Cellular Biology*, 14, 1972-1978.

Inglis, D.O., Amaud, M.B., Binkley, J., Shah, P., Skrzypek, M.S., Wymore, F., … Sherlock, G. (2012). The *Candida* genome database incorporates multiple *Candida* species multiple search and analysis tools with curated gene and protein information for *Candida albicans* and *Candida glabrata*. *Nucleic Acids Research*, 40, D667-674.

Iraqui, I., Garcia-Sanchez, S., Aubert, S., Dromer, F., Ghigo, J.M., d'Enfert, C., & Janbon, G. (2005). The Yak1p kinase controls expression of adhesins and biofilm in *Candida glabrata* in a Sir4p-dependent pathway. *Molecular Microbiology*, 55, 1259-1271.

Jacobsen, I.D., Brunke, S., Seider, K., Schwarzmüller, T., Firon, A., d'Enfért, C., … Hube, B. (2010). *Candida glabrata* persistence in mice does not depend on host immunosuppression and is unaffected by fungal amino acid auxotrophy. *Infection and Immunity*, 78, 1066-1077.

Johnston, M. (1999). Feasting, fasting and fermentating: Glucose sensing in yeast and other cells. *Trends in Genetics*, 15, 29-33.

Johnston, M., & Kim, J.H. (2005). Glucose as a hormone: Receptor-mediated glucose sensing in the yeast *Saccharomyces cerevisiae*. *Biochemical Society Transactions*, 33, 247-252.

Jouandot, D, 2nd, Roy, A., & Kim, J.H. (2011). Functional dissection of the glucose signaling pathways that regulate the yeast glucose transporter gene (*HXT*) repressor Rgt1. *Journal of Cellular Biochemistry*, 112, 3268-3275.

Kaloriti, D., Jacobsen, M.D, Yin, Z., Patterson, M., Tillmann, A.T, Smith, D.A., … Brown, A.J. (2014). Mechanism underlying the exquisite sensitivity of *Candida albicans* to combinatorial cationic and oxidative stress that enhances the potent fungicidal activity of phagocytes. *mBio*, 5, e01334-e01314.

Kaniak, A., Xue, Z., Macool, D., Kim, J.H., & Johnston, M. (2004). Regulatory network connecting two glucose signal transduction pathways in *Saccharomyces cerevisiae*. *Eukaryotic Cell*, 3, 221-231.

Káposzta, R., Maródi, L., Hollinshead, M., Gordon, S., & da Silva, R.P. (1999). Rapid recruitment of late endosome and lysosomes in mouse macrophages ingesting *Candida albicans*. *Journal of Cell Science*, 112, 3237-3248.

Karaböcüoglu, M., Sökücü, S., Gökcay, G., Ucsel, R., & Neyzi, O. (1994). Carbohydrate malabsorption in acute diarrhea. *Indian Pediatrics*, 31, 1071-1074.

Karhumaa, K., Wu, B., & Kielland-Brandt, M.C. (2010). Conditions with high intracellular glucose inhibit sensing through glucose sensor Snf3 in *Saccharomyces cerevisiae*. *Journal of Cellular Biochemistry*, 110, 920-925.

Katiyar, S.K., Alastruey-Izquierdo, A., Healey, K.R., Johnson, M.E., Perlin, D.S., & Edlind, T.D. (2012). Fks1 and Fks2 are functionally redundant but differentially regulated in *Candida glabrata*: implications for echinocandin resistance. *Antimicrobial Agents and Chemotherapy*, 56, 6304-6309.

Kaur R., Domergue, R., Zupancic, M.L., & Cormack, B.P. (2005). A yeast by any other name: *Candida glabrata* and its interaction with the host. *Current opinion in Microbiology*, 8, 378-384.

Kaur, R., Ma, B., & Cormack, B.P. (2007). A family of glycosylphosphatidylinositol-linked aspartyl proteases is required for virulence of *Candida glabrata*. *Proceedings of the National Academy of Sciences of the United States of America*, 104, 7628-7633.

Kim, J.H., Polish, J., & Johnston, M. (2003). Specificity and regulation of DNA binding by the yeast glucose transporter gene repressor Rgt1. *Molecular and Cellular Biology*, 23, 5208-5216.

Kojic, E.M., & Darouiche, R.O. (2004). *Candida* infections of medical devices. *Clinical Microbiology Reviews*, 17, 255-267.

Komalapriya, C., Kaloriti, D., Tillmann, A.T., Yin, Z., Herrero-de-Dios, C., Jacobsen, M.D., … Romano, C.M. (2015). Integrative model of oxidative stress adaptation in the fungal pathogen *Candida albicans*. *PLoS ONE*, 10, e0137750.

Kruckeberg, A.L. (1996). The hexose transporter family of *Saccharomyces cerevisiae*. *Archives of Microbiology*, 165, 283-292.

Kuhn, D.M., Chandra, J., Mukherjee, P.K., & Ghannoum, M.A. (2002a). Comparison of biofilms formed by *Candida albicans* and *Candida parapsilosis* on bioprosthetic surfaces. *Infection and Immunity*, 70, 878-888.

Kuhn, D.M., George, T., Chandra, J., Mukherjee, P.K., & Ghannoum, M.A. (2002b). Antifungal susceptibility of *Candida* biofilms: Unique effifcacy of amphotericin B lipid formulations and echinocandins. *Antimicrobial Agents and Chemotherapy*, 46, 1773-1780.

Lakshmanan, J., Mosley, A.L., & Özcan, S. (2003). Repression of transcription by Rgt1 in the absence of glucose requires Std1 and Mth1. *Current Genetics*, 44, 19-25.

Li, Q.Q., Skinner, J., & Bennett, J.E. (2012). Evaluation of reference genes for real-time quantitative PCR studies in *Candida glabrata* following azole treatment. *BMC Molecular Biology*, 13, 22.

Liang, H., & Gaber, R.F. (1996). A novel signal transduction pathway in *Saccharomyces cerevisiae* defined by Snf3-regulated expression of *HXT6*. *Molecular Biology of the Cell*, 7, 1953-1966.

Lin, C.Y., Chen, Y.C., Lo, H.J., Chen, K.W., & Li, S.Y. (2007). Assessment of *Candida glabrata* relatedness by pulsed-field gel electrophoresis and multilocus sequence typing. *Journal of Clinical Microbiology*, 45, 2452-2459.

Lin, M.Y., Carmeli, Y., Zumsteg, J., Flores, E.L., Tolentino, J., Sreeramoju, P., & Weber, S.G. (2005). Prior antimicrobial therapy and risk for hospital-acquired *Candida glabrata* and *Candida krusei* fungemia: a case-case-control study. *Antimicrobial Agents Chemotherapy*, 49, 4555-4560.

Liu, T.T., Lee, R.E., Barker, K.S., Lee, R.E., Homayouni, R., & Rogers, P.D. (2005). Genome-wide expression profiling of the response to azole, polyene, echinocandin, and pyrimidine antifungal agents in *Candida albicans*. *Antimicrobial Agents Chemotherapy*, 49, 2226-2236.

Liu, T.B., Wang, Y., Baker, G.M., Fahmy, H., Jiang, L., & Xue, C. (2013). The glucose sensor-like protein Hxs1 is a high-affinity glucose transporter and required for virulence in *Cryptococcus neoformans*. *PLoS ONE*, 8, e64239.

Lorenz, M.C., Bender, J.A., & Fink, G.R. (2004). Transcriptional response of *Candida albicans* upon internalization by macrophages. *Eukaryotic Cell*, 3, 1076-1087,

Lundin, M., Nehlin, J.O., & Ronne, H. (1994). Importance of a flanking AT-rich region in target site recognition by the GC box-binding zinc finger protein *MIG1*. *Molecular and Cellular Biology*, 14, 1979-1985.

Luo, L., Tong, X., & Farley, P.C. (2007). The *Candida albicans* gene *HGT12* (orf19.7094) encodes a hexose transporter. *FEMS Immunology and Medical Microbiology*, 51, 14-17.

Luongo, M., Porta, A., & Maresca, B. (2005). Homolog, disruption and phenotypic analysis of CaGS *Candida albicans* gene induced during macrophage infection. *FEMS Immunology and Medical Microbiology*, 45, 471-478.

Lutfiyya, L.L., Iyer, V.R., DeRisi, J., DeVit, M.J., Brown, P.O., & Johnston, M. (1998). Characterization of three related glucose repressors and genes they regulate in *Saccharomyces cerevisiae*. *Genetics*, 150, 1377-1391.

Lutfiyya, L.L., & Johnston, M. (1996). Two zinc-finger-containing repressors are responsible for glucose repression of *SUC2* expression. *Molecular and Cellular Biology*, 16, 4790-4797.

Ma, H., Croudace, J.E., Lammas, D.A., & May, R.C. (2006). Explusion of live pathogenic yeast by macrophages. *Current Biology*, 16, 2156-2160.

Maier, A., Völker, B., Boles, E., & Fuhrmann, G.F. (2002). Characterisation of glucose transport in *Saccharomyces cerevisiae* with plasma membrane vesicles (countertransport) and intact cells (initial uptake) with single Hxt1, Hxt2, Hxt3, Hxt4, Hxt6, Hxt7 or Gal2 transporters. *FEMS Yeast Research*, 2, 539-550.

Malani, A., Hmoud, J., Chiu, L., Carver, P.L., Bielaczyz, A., & Kauffman C.A. (2005). *Candida glabrata* fungemia: experience in a tertiary care center. *Clinical Infectious Diseases*, 41, 975-981.

Mansour, M.K., & Levitz, S.M. (2002). Interactions of fungi with phagocytes. *Current Opinion in Microbiology*, 5, 359-365.

Marcil, A., Harcus, D., Thomas, D.Y., & Whiteway, M. (2002). *Candida albicans* killing by RAW 264.7 mouse macrophage cells: effect of *Candida* genotype, infection ratios, and gamma interferon treatment. *Infection and Immunity*, 70, 6919-6929.

Martinez, L.R., & Casadevall, A. (2007). *Crytococcus neoformans* biofilm formation depends on surface support and carbon susceptibility to hear, cold, and UV light. *Applied and Environmental Microbiology*, 73, 4592-4601.

McWilliam, H., Li, W., Uludag, M., Squizzato, S., Park, Y.M., Buso, N., … Lopez, R. (2013). Analysis tool web services from the EMBL-EBI. *Nucleic Acids Research*, 41,W597-600.

Mercado, J.J., Smith, R., Sagilocco, F.A., Brown, A.J., & Gancedo, J.M. (1994). The levels of yeast gluconeogenic mRNAs respond to environmental factors. *European Journal of Biochemistry*, 224, 473-481.

Miwa, T., Takagi, Y., Shinozaki, M., Yun, C.W., Schell, W.A., Perfect, J.A., … Tamaki, H. (2004). Gpr1, a putative G-protein-coupled receptor, regulates morphogenesis and hypha formation in the pathogenic fungus *Candida albicans*. *Eukaryotic Cell*, 3, 919-931.

Molero, G., Diez-Orejas, R., Navarro-García, F., Monteoliva, L., Pia, J., Gil, C., … Nombela, C. (1998). *Candida albicans*: Genetics, dimorphism and pathogenicity. *International Microbiology*, 1, 95-106.

Mora-Duarte, J., Betts, R., Rotstein, C., Colombo, L.A, Thompson-Moya, L., Smietana, J., … Perfect, J. (2002). Comparison of caspofungin and amphotericin B for invasive candidiasis. *New England Journal of Medicine*, 347, 2020-2029.

Moriya, H., & Johnston, M. (2004). Glucose sensing and signaling in *Saccharomyces cerevisiae* through the Rgt2 glucose sensor and casein kinase I. *Proceedings of the National Academy of Sciences of the United States of America*, 101, 1572-1577.

Mosley, A.L., Lakshmanan, J., Aryal, B.K., & Özcan, S. (2003). Glucose-mediated phosphorylation converts the transcription factor Rgt1 from a repressor to an activator. *The Journal of Biological Chemistry*, 278, 10322-10327.

Mukherjee, P.K., & Chandra, J. (2004). *Candida* biofilm resistance. *Drug Resistance Update*, 7, 301-309.

Muller, H., Hennequin, C., Gallaud, J., Dujon, B., & Fairhead, C. (2008). The asexual yeast *Candida glabrata* maintains distinct a and α haploid mating types. *Eukaryotic cell*, 7, 848-858.

Murima, P., McKinney, J.D., Pethe, K. (2014). Targeting bacterial central metabolism for drug development. *Chemistry & Biology*, 21, 1423-1432.

Myers, R.L. (2007). *The 100 most important chemical compounds: A reference guide*. Westport: Greenwood Publishing Group.

Nagayoshi, Y., Miyazaki, T., Minematsu, A., Yamauchi, S., Takazono, T., Nakamura, S., … Kohno, S. (2014). Contribution of the Slt2-regulated transcription factors to echinocandin tolerance in *Candida glabrata*. *FEMS Yeast Research*, 14, 1128-1131.

National Committee for Clinical Laboratory Standards. (2002). *Reference method for broth dilution antifungal susceptibility testing of yeasts: Approved standard M27-A2*. Pennsylvania, PA: National Committee for Clinical Laboratory Standards.

Ng, K.P., Kuan, C.S., Kaur, H., Na, S.L., Atiya, N., & Velayuthan, R.D. (2015). *Candida* species epidemiology 2000-2013: A laboratory-based report. *Tropical Medicine and International Health*, 20, 1447-1453.

Ng, K.P., Madasamy, M., Saw, T.L., Baki, A., He, J., & Soo-Hoo, T.S. (1999). *Candida* biotypes isolated from clinical specimens in Malaysia. *Mycopathologia*, 144, 135-140.

Nikolaou, E., Agrafioti, I., Stumpf, M., Quinn, J., Stanfield, I., & Brown, A.J. (2009). Phylogenetic diversity of stress signaling pathways in fungi. *BMC Evolutionary Biology*, 9, doi: 10.1186/1471-2148-9-44.

Nourani, A., Wesolowski-Louvel, M., Delaveau, T., Jacq, C., & Delahodde, A. (1997). Multiple-drug-resistance phenomenon in the yeast *Saccharomyces cerevisiae*: Involvement of two hexose transporters. *Molecular and Cellular Biology*, 17, 5453-5460.

Odds, F.C., Brown, A.J., & Gow, N.A. (2003). Antifungal agents: Mechanisms of action. *Trends in Microbiology*, 11, 272-279.

Odds, F.C., Gow, N.A., & Brown, A.J. (2006). Toward a molecular understanding of *Candida albicans* virulence. In Heitman, J., Filler, S.G., Edwards, Jr., & Mitchell, A.P. (Eds.), *Molecular Principles of Fungal Pathogenesis*. (pp. 3-11). Washington, DC: American Society of Microbiology.

Osherov, N., May, G.S., Albert, N.D., & Kontoyiannis, D.P. (2002). Overexpression of Sbe2p, a Golgi protein, results in resistance to caspofungin in *Saccharomyces cerevisiae*. *Antimicrobial Agents and Chemotherapy*, 46, 2462-2469.

Özcan, S., Leong, T., & Johnston, M. (1996a). Rgt1p of *Saccharomyces cerevisiae*, a key regulator of glucose-induced genes, is both an activator and a repressor of transcription. *Molecular and Cellular Biology*, 16, 6419-6426.

Özcan, S., Dover, J., & Johnston, M. (1998). Glucose sensing and signaling by two glucose receptors in the yeast *Saccharomyces cerevisiae*. *The EMBO Journal*, 17, 2566-2573.

Özcan, S., Dover, J., Rosenwald, A.G., Wölfl, S., & Johnston, M. (1996b) Two glucose transporters in *Saccharomyces cerevisiae* are glucose sensors that generate a signal for induction of gene expression. *Proceedings of the National Academy of Sciences of the United States of America*, 93, 12428-12432.

Özcan, S., & Johnston, M. (1995). Three different regulatory mechanisms enable yeast hexose transporter (*HXT*) genes to be induced by different levels of glucose. *Molecular and Cellular Biology*, 15, 1564-1572.

Özcan, S., & Johnston, M. (1999). Function and regulation of yeast hexose transporters. *Microbiology and Molecular Biology Reviews*, 63, 554-569.

Palma, M., Seret, M.L., & Baret, P.V. (2009). Combined phylogenetic and neighbourhood analysis of the hexose transporter and glucose sensors in yeasts. *FEMS Research Research*, 9, 526-534.

Pappas, P.G., Kauffman, C.A., Andes, D., Benjamin, D.K.Jr., Calandra, T.F., Edwards, J.E.Jr., … Infectious Diseases Society of America. (2009). Clinical practice guidelines for the management of candidiasis: 2009 update by the Infectious Diseases Society of America. *Clinical infectious Diseases*, 48, 503-535.

Paul, S., Schimdt, J.A., & Moye-Rowley, W.S. (2011). Regulation of the CgPdr1 transcription factor from the pathogen *Candida glabrata*. *Eukaryotic Cell*, 10, 187-197.

Perfect, J.R. (2016). Is there an emerging need for new antifungals? *Expert Opinion on Emerging Drugs*, in press, doi:10.1517/14728214.2016.1155554.

Perfect, J.R., & Casadevall, A. (2006). Fungal molecular pathogenesis: What can it do and why do we need it? In Heitman, J., Filler, S.G., Edwards, Jr., & Mitchell, A.P. (Eds.), *Molecular Principles of Fungal Pathogenesis*. (pp. 305-319). Washington, DC: American Society of Microbiology.

Perlin, D.S. (2007). Resistance to echinocandin-class antifungal drugs. *Drug Resistance Updates*, 10, 121-130.

Pfaffl, M.W. (2001). A new mathematical model for relative quantification in real-time RT-PCR. *Nucleic Acids Research*, 29, e45.

Pfaffl, M.W., Horgan, G.W., & Dempfle, L. (2002). Relative expression software tool (REST) for group-wise comparison and statistical analysis of relative expression results in real-time PCR. *Nucleic Acids Research*, 30, e36.

Pfaller, M.A., & Diekema, D. J. (2007). Epidemiology of invasive candidiasis: A persistent public health problem. *Clinical Microbiology Reviews*, 20, 133-163.

Pfaller, M.A., & Castanheira, M. (2016). Nosocomial candidiasis: Antifungal stewardship and the importance of rapid diagnosis. *Medical Mycology*, 54, 1-22.

Pfaller, M.A., Andes, D.R., Diekema, D.J., Horn, D.L., Reboli, A.C., Rotstein, C., & Azie, N.E. (2014). Epidemiology and outcomes of invasive candidiasis due to non-*albicans* species of *Candida* in 2496 patients: Data from the prospective antifungal therapy (PATH) registry 2004-2008. *PLoS ONE*, 9, e101510.

Pfaller, M.A., Castanheira, M., Lockhart, S.R., Ahlquist, A.M., Messer, S.A., & Jones, R.N. (2012). Frequency of descreased susceptibility and resistance to echinocandins among fluconazole-resistant bloodstream isolates of *Candida glabrata*. *Applied and Environmental Microbiology*, 50, 1199-1203.

Pfaller, M.A., Diekema, D.J., Gibbs, D.L., Newell, V.A., Ellis, D., Tullio, V., … the Global Antifungal Surveillance Group. (2010). Result from the ARTEMIS DISK Global Antifungal Surveillance Study, 1997 to 2007: A 10.5-Year analysis of susceptibilities of *Candida* species to Fluconazole and Voriconazole as determined by CLSI standardized disk diffusion. *Journal of Clinical Microbiology*, 48, 1366-1377.

Pierce, C.G., Uppuluri, P., Tristan, A.R., Wormley, F.L.Jr., Mowat, E., Ramage, G., & Lopez-Ribot, J.L. (2008). A simple and reproducible 96-well plate-based method for the formation of fungal biofilms and its application to antifungal susceptibility testing. *Nature Protocols*, 3, 1494-1500.

Piškur, J., Rozpedowska, E., Polakova, S., Merico, A., & Compagno, C. (2006). How did *Saccharomyces* evolve to become a good brewer? *Trends in Genetics*, 22, 183-186.

Poláková, S., Blume, C., Zárate, J.Á., Mentel, M., Jøcrk-Ramberg, D., Stenderup, J., & Piškur, J. (2009). Formation of new chromosomes as a virulence mechanism in yeast *Candida glabrata*. *Proceedings of the National Academy of Sciences of the United States of America*, 106, 2688-2693.

Polish, J.A., Kim, J.H., & Johnston, M. (2005). How the Rgt1 transcription factor of *Saccharomyces cerevisiae* is regulated by glucose. *Genetics*, 169, 583-594.

Prior, C., Fukuhara, H., Blaisonneau, J., & Wesolowski-Louvel, M. (1993). Low-affinity glucose carrier gene *LGT1* of *Saccharomyces cerevisiae*, a homologue of the *Kluyveromyces lactis RAG1* gene. *Yeast*, 9, 1373-1377.

Pronk, J.T., Yde Steensma., H., & van Dijken, J. (1996). Pyruvte metabolism in *Saccharomyces cerevisiae*. *Yeast*, 12, 1607-1633.

Puissant, C., & Houdebine, L.M. (1990). An improvement of the single-step method of RNA isolation by acid guanidinium thiocyanate-phenol-chloroform extraction. *BioTechniques*, 8, 148-149.

Rai, M.N., Balusu, S., Gorityala, N., Dandu, L., & Kaur, R. (2012). Functional genomic analysis of *Candida glabrata*-macrophage interaction: role of chromatin remodeling in virulence. *PLoS Pathogens*, 8, e1002863.

Rajendran, R., Sherry, L., Nile, C.J., Sherriff, A., Johnston, E.M., Hanson, M.F., … Ramage, J.G. (2016). Biofilm formation is a risk factor for mortality in patients with *Candida albicans* bloodstream infection – Scotland, 2012 – 2013. *Clinical Microbiology and Infection*, 22, 87-93.

Ramage, G., Saville, S.P., Thomas, D.P., & López-Ribot, J.L. (2005). *Candida* biofilms: An update. *Eukaryotic Cell*, 4, 633-638.

Ramage, G., Mowat, E., Williams, C., Lopez Ribot. (2010). Chapter 6: Yeast Biofilms. In Ashbee, H.R & Bignell, E.M. (Eds), *Pathogenic Yeasts, The Yeast Handbook*. (pp. 121-143). Berlin Heidelberg: Spinger-Verlag.

Ramos, J., Szkutnicka, K., & Cirillo, V.P. (1988). Relationship between low- and high-affinity glucose transport system of *Saccharomyces cerevisiae*. *Journal of Bacteriology*, 170, 5375-5377.

Reboli, A.C., Rostein, C., Pappas, P.G., Chapman, S.W., Kett, D.H., Kumar, D., … Walsh, T.J. (2007). Anidulafungin versus fluconazole for invasive candidiasis. *New England Journal of Medicine*, 356, 2472-2482.

Reifenberger, E., Boles, E., & Ciriacy, M. (1997). Kinetic characterization of individual hexose transporters of *Saccharomyces cerevisiae* and their relation to the mechanisms of glucose repression. *European Journal of Biochemistry*, 245, 324-333.

Resuehr, D., & Spiess, A.N. (2003). A real-time polymerase chain reaction-based evalution of cDNA synthesis priming methods. *Analytical Biochemistry*, 322, 287-291.

Ren, B., Robert, F., Wyrick, J.J., Aparicio, O., Jennings, E.G., Simon, I., … Young, R.A. (2000). Genome-wide location and function of DNA binding proteins. *Science*, 290, 2306-2309.

Ricardson, M.D. (1991). Opportunistic and pathogenic fungi. *The Journal of Antimicrobial Chemotherapy*, 28, 1-11.

Robinson, L.C., Hubbard, E.J., Graves, P.R., DePaoli-Roach, A.A., Roach, P.J., Kung, C., … Carlson, M. (1992). Yeast casein kinase I homologues: an essential gene pair. *Proceedings of the National Academy of Sciences of the United States of America*, 89, 28-32.

Rodaki, A., Bohovych, IM., Enjalbert, B., Young, T., Odds, F.C., Gow, N.A., & Brown, A.J. (2009). Glucose promotes stress resistance in the fungal pathogen *Candida albicans*. *Molecular Biology of the Cell*, 20, 4845-4855.

Roetzer, A., Gabaldón, T., & Schűller, C. (2011). From *Saccharomyces cerevisiae* to *Candida glabrata* in a few easy steps: Important adaptations for an opportunistic pathogen. *FEMS Microbiology Letters*, 314, 1-9.

Roezter, A., Gratz, N., Kovarik, P., & Schüller, C. (2010). Autophagy supports *Candida glabrata* survival during phagocytosis. *Cellular Microbiology*, 12, 199-216.

Rolland, F., Winderickx, J., & Thevelein, J.M. (2002). Glucose-sensing and –signalling mechanism in yeast. *FEMS Yeast Research*, 2, 183-201.

Rusche, L.N., Kirchmaier, A.L., & Rine, J. (2003). The establishment, inheritance, and function of silenced chromatin in *Saccharomyces cerevisae*. *Annual Review of Biochemistry*, 72, 481-516.

Sabina, J., & Brown, V. (2009). Glucose sensing network in *Candida albicans*: a sweet spot for fungal morphogenesis. *Eukaryotic Cell*, 8, 1314-1320.

Sambrook, J., & Rusel, D. (2001). *Molecular cloning: A laboratory manual. 3rd ed.* Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York.

Sampiao, P., & Pais, C. (2014). Epidemiology of invasive candidiasis and challenges for the mycology laboratory: Specificities of *Candida glabrata*. *Currrent Clinical Microbiology Reports*, 1, 1-9.

Sandai, D., Yin, Z., Selway, L., Steed, D., Walker, J., Leach, M.D., … Brown, A.J. (2012). The evolutionary rewiring of ubiquitination targets has reprogrammed the regulation of carbon assimilation in the pathogenic yeast *Candida albicans*. *mBio*, 3, e00495

Sanglard, D. (2002). Resistance of human fungal pathogens to antifungal drugs. *Current Opinon in Microbiology*, 5, 379-385.

Sanglard, D., Ischer, F., & Bille, J. (2001). Role of ATP-binding-cassette transporter genes in high-frequency acquisition of resistance to azole antifungals in *Candida glabrata*. *Antimicrobial Agents and Chemotherapy*, 45, 1174-1183.

Sanguinetti, M., Posteraro, B., Ranno, S., Torelli, R., & Fadda, G. (2005). Mechanisms of azole resistance in clinical isolates of *Candida glabrata* collected during a hospital survey of antifungal resistance. *Antimicrobial Agents and Chemotherapy*, 49, 668-679.

Santangelo, G.M. (2006). Glucose signaling in *Saccharomyces cerevisiae*. *Microbiology and Moleular Biology Reviews*, 70, 253-282.

Schüller, H.J. (2003). Transcriptional control of nonfermentative metabolism in the yeast *Saccharomyces cerevisiae*. *Current Genetics*, 43, 139-160.

Seider, K., Brunke, S., Schild L., Jablonowski, N., Wilson, D., Majer, O., … Hube, B. (2011). The facultative intracellular pathogen *Candida glabrata* subverts macrophage cytokine production and phagolysosome maturation. *The Journal of Immunology*, 187, 3072-3086.

Seneviratne, C.J., Silva, W.J., Jin, L.J., Samaranayake, Y.H., & Samaranayake, L.P. (2009). Architectural analysis, viability assessment and growth kinetics of *Candida albicans* and *Candida glabrata* biofilms. *Archive of Oral Biology*, 54, 1052-1060.

Serrano-Fujarte, I., López-Romero, E., Reyna-López, G,E., Martínez-Gámez, M.A., Vega-González, A., & Cuéllar-Cruz, M. (2015). Influence of culture media on biofilm formation *Candida* species and response of sessile cells to antifungals and oxidative stress. *BioMed Research International*. Vol. 2015. doi:10.1155/2015/783639.

Sexton, J.A., Brown, V., & Johnston, M. (2007). Regulation of sugar transport and metabolism by *Candida albicans* Rgt1 transcriptional repressor. *Yeast*, 24, 847-860.

Sherman, F. (2002). Getting started with yeast. *Methods in Enzymology*, 350, 3-41.

Shin, J.H., Kee, S.J., Shin, M.G., Kim, S.H., Shin, D.H., Lee, S.K., … Ryang, D.W. (2002). Biofilm production by isolates of *Candida* species recovered from nonneutropenic patients: comparison of bloodstream isolates with isolates from other sources. *Journal of Clinical Microbiology*, 40, 1244-1248.

Shin, J.H., Chae, M.J., Song, J.W., Jung S.I., Cho, D., Kee, S.J., … Ryang, D.W. (2007). Changes in karyotype and azole susceptibility of sequential bloodstream isolates form patients with *Candida glabrata* candidemia. *Journal of Clinical Microbiology*, 45, 2385-2391.

Sickmann, A., Reinders, J., Wagner, Y., Joppich, C., Zahedi, R., Meyer, H.E., … Meisinger, C. (2003). The proteome of *Saccharomyces cerevisiae* mitochondria. *Proceedings of the National Academy of Sciences of the United Stated of America*, 100, 13207-13212.

Sievers, F., Wilm, A., Dineen, D., Gibson, T.J., Karplus, K., Li, W., … Higgins, D.G. (2011). Fast, scalable generation of high-quality protein multiple sequence alignments using Clustal Omega. *Molecular Systems Biology*, 7, 539

Silva-Dias, A., Miranda, I.M., Branco, J., Monteiro-Soares, M., Pina-Vaz, C., & Rodrigues, A.G. (2015). Adhesion, biofilm formation, cell surface hydrophobicity, and antifungal planktonic susceptibility: Relationship among *Candida* spp. *Frontiers in Microbiology*, 6, 205.

Silva, S., Henriques, M., Hayes, A., Oliveira, R., Azeredo, J., & Williams D.W. (2011b). *Candida glabrata* and *Candida albicans* co-infection of an *in vitro* oral epithelium. *Journal of Oral Pathology Medicine*, 40, 421-427.

Silva, S., Negri, M., Henriques, M., Oliveira, R., Williams, D.W., & Azeredo, J. (2011a). Adherence and biofilm formation of non-*Candida albicans Candida* species. *Trends in Microbiology*, 19, 241-247.

Singh-Babak, S.D., Babak, T., Diezmann, S., Hill, J.A., Xie, J.L., Chen, Y.L., … Cowen, L.E. (2012). Global analysis of the evolution and mechanism of echinocandin resistance in *Candida glabrata*. *PLoS Pathogens*, 8, e1002718.

Spielewoy, N., Flick, K., Kalashnikova, T.I., Walker, J.R., & Wittenberg, C. (2004). Regulation and recognition of SCFGrr1 targets in the glucose and amino acid signaling pathways. *Molecular and Cellular Biology*, 24, 8994-9005.

Srikantha, T., Lachke, S. A., & Soll, D. R. (2003). Three mating type-like loci in *Candida glabrata*. *Eukaryotic cell*, 2, 328-340.

Stanhill, A., Schick, N., & Engelberg, D. (1999). The yeast ras/cyclic AMP pathway induced growth by suppressing the cellular stress response. *Molcular and Cellular Biology*, 19, 7529-7538.

Sun, L., Zeng, X., Yan, C., Sun, X., Gong, X., Rao, Y., & Yan, N. (2012). Crystal structure of a bacterial homologue of glucose transporters *GLUT1-4*. *Nature*, 490, 361-366.

Tamura, K., Peterson, D., Peterson, N., Stecher, G., Nei, M., & Kumar, S. (2011). MEGA5: molecular evolutionary genetics analysis using maximum likelihood, evolutionary distance, and maximum parsimony methods. *Molecular Biology and Evolution*, 28, 2731-2739.

Tan, T.Y., Hsu, L.Y., Alejandria, M.M., Chaiwarith, R., Chinniah, T., Chayakulkeeree, M., … Pham, H.V. (2016). Antifungal susceptibility of invasive *Candida* bloodstream isolates from the Asia-Pacific region. *Medical Mycology*, 54, 471-477.

Tay, S. T., Lotfalikhani, A., Sabet, N. S., Ponnampalavanar, S., Sulaiman, S., Na, S. L., & Ng, K. P. (2014). Occurrence and characterstization of *Candida nivariensis* from a culture collection of *Candida glabrata* clinical isolates in Malaysia. *Mycopathologia*, 178, 307-14.

Thevelein, J.M., & de Winde, J.H. (1999). Novel sensing mechanism and targets for the cAMP-protein kinase A pathway in the yeast *Saccharomyces cerevisiae*. *Molecular Microbiology*, 33, 904-918.

Thierry, A., Bouchier, C., Dujon, B., & Richard G. F. (2008). Megasatelite: a peculiar class of giant minisatelite in genes invloved in cell adhesion and pathogenicity in *Candida glabrata*. *Nucleic Acids Research*, 36, 5970-5982.

Thomson, E., Ferreira-Cerca, S., & Hurt, E. (2013). Eukaryotic ribosome biogenesis at a glance. *Journal of Cell Science*, 126, 4815-4821.

Thön, M., Al-Abdallah, Q., Hortschansky, P., & Brakhage, A.A. (2007). The thioredoxin system of the filamentous fungus *Aspergillus nidulans*: Impact on development and oxidative stress response. *The Journal of Biological Chemistry*, 282, 27259-27269.

Towle, H.C. (2005). Glucose as a regulator of eukaryotic gene transcription. *Trends in Endocrinology and Metabolism*, 16, 489-494.

Tsai, H.F., Krol, A.A., Sarti, K.E., & Bennett, J.E. (2006). *Candida glabrata PDR1*, a transcriptional regulator of a pleiotropic drug resistance network, mediates azole resistance in clinical isolates and petite mutants. *Antimicrobial Agents and Chemotherapy*, 50, 1384-1392.

Uppuluri, P., Chatuverdi, A.K., Srinivasan, A., Banerjee, M., Ramasubramaniam, A.K., Köhler, J.R., … Lopez-Ribot, J.L. (2010). Dispersion as an important step in the *Candida albicans* biofilm developmental cycle. *PLoS Pathogens*, 6, e1000828.

Vallier, L.G., & Carlson, M. (1994). Synergistic release from glucose repression by *MIG1* and *SSN* mutations in *Saccharomyces cerevisiae*. *Genetics*, 137, 49-54.

van der Graaf, C.A., Netea, M.G., Verschueren, I., van der Meer, J.W., & Kullberg, B.J. (2005). Differential cytokine production and toll-like receptor signaling pathways by *Candida albicans* blastoconidia and hyphae. *Infection and Immunity*, 73, 7458-7464.

van Urk, H., Voll, W.S.L., Scheffers, W.A., & van Dijken, J.P. (1990). Transcient-state analysis of metabolic fluxes in crabtree-positive and crabtree-negative yeasts. *Applied and Environmental Microbiology*, 56, 281-287.

Veira, O.V., Botelho, R.J., & Grinstein, S. (2002). Phagosome maturation: aging gracefully. *Biochemical Journal*, 366, 689-704.

Vermitsky, J.P., & Edlind, T.D. (2004). Azole resistance in *Candida glabrata*: coordinate upregulation of multidrug transporters and evidence for a Pdr1-like transcription factor. *Antimicrobial Agents and Chemotherapy*, 48, 3773-3781.

Verwaal, R, Arako, M., Kapur, R., Verkleij, A.J., Verrips, C.T., & Boonstra, J. (2004). *HXT5* expression is under control of STRE and HAP elements in the *HXT5* promoter. *Yeast*, 21, 747-757.

Verwaal, R., Paalman, J.W., Hogenkamp, A., Verkleij, A.J., Verrips, C.T., & Boonstra, J. (2002). *HXT5* exprssion is determined by growth rates in *Saccharomyces cerevisiae*. *Yeast*, 19, 1029-1038.

Villena, S.N., Pinheiro, R.O., Pinheiro, C.S., Nunes, M.P., Takiya, C.M., DosReis, G.A., … Freire-de-Lima, C.G. (2008). Capsular polysaccharides galactoxylomannan and glucuronoxylomannan from *Cryptococcus neoformans* induce macrophage apoptosis mediated by Fas ligand. *Cellular Microbiology*, 10, 1274-1285.

Walter III, M.C., Roe, F., Bugnicourt, A., Franklin, M.J., & Stewart, P.S. Contributions of antibiotic penetration, oxygen limitation, and low metabolic activity to tolerance of *Pesudomonas aeruginosa* biofilms to ciprofloxacin and tobramycin. *Antimicrobial Agents and Chemotherapy*, 47, 317-323.

Wang, Y., Pierce, M., Schneper, L., Güldal, C.G., Zhang, X., Tavazole, S., & Broach, J.R. (2004). Ras and Gpa2 mediate one brance of a redundant glucose signalling pathway in yeast. *PLoS Biology*, 2, E128.

Wellington, M., Dolan, K., & Krysan, D.J. (2009). Live *Candida albicans* suppresses production of reactive oxygen species in phagocytes. *Infection and Immunity*, 77, 405-413.

Westholm, J.O., Nordberg, N., Murén, E., Ameur, A., Komorowski, J., & Ronne, H. (2008). Combinatorial control of gene expression by the three yeast repressors Mig1, Mig2, and Mig3. *BMC Genomics*, 9, 601.

Weusthuis, R.A., Pronk, J.T., van den Broek, P.J., & van Dijken, J.P. (1994). Chemostat cultivation as a tool for studies on sugar transport in yeasts. *Microbiological Reviews*, 58, 616-630.

Widdel, F. (2010). Theory and measurement of bacterial growth. University of Bremen. Retrieved from:www.mpi-bremen.de/Binaries/Binary13037/Wachstumsversuch.pdf.

Wieczorke, R., Krampe, S., Weierstall, T., Freidel, K., Hollenberg, C.P., & Boles, E. (1999). Concurrent knock-out of at least 20 transporter genes is required to block uptake of hexoses in *Saccharomyces cerevisiae*. *FEBS Letters*, 464, 123-128.

Willems, A.R., Schwab, M., & Tyers, M. (2004). A hitchhiker's guide to the cullin ubiquitin ligases: SCF and its kin. *Biochimica et Biophysica Acta*, 1695, 133-170.

Wilson, L.S., Reyes, C.M., Stolpman, M., Speckman, J., Allen, K., & Beney, J. (2002). The direct cost and incidence of systemic fungal infections. *Value in Health*, 5, 26-34.

Wisplinghoff, H., Bischoff, T., Tallent, S.M., Seifert, H., Wenzel, R.P., & Edmond, M.B. (2004). Nosocomial bloodstream infections in US hospitals: analysis of 24,179 cases from a prospective nationwide surveillance study. *Clinical Infectious Diseases*, 39, 309-317.

Wotton, D., & Shore, D. (1997). A novel Rap1p-interacting factor, Rif2p, cooperates with Rif1p to regulate telomere length in *Saccharomyces cerevisiae*. *Genes & Development*, 11, 748-760.

Xu, N., Liu, L., Zou, W., Liu, J., Hua, Q., & Chen, J. (2013). Reconstruction and analysis of the genome-scale metabolic network of *Candida glabrata*. *Molecular BioSystem*, 9, 205.

Ye, L., Berden, J.A., van Dam, K., & Kruckeberg, A.L. (2001). Expression and activity of the Hxt7 high-affinity hexose transporter of *Saccharomyces cerevisiae*. *Yeast*, 18, 1257-1267.

Yin, Z., Wilson, S., Hauser, N.C., Tournu, H., Hoheisel, J.D., & Brown, A.J. (2003). Glucose triggers different global responses in yeast, depending on the strength of the signal, and transiently stabilizes ribosomal protein mRNAs. *Molecular Microbiology*, 48, 713-724.

Zaas, A.K., & Alexander, B.D. (2005). Echinocandins: role in antifungal therapy. *Expert Opinion on Pharmacotherapy*, 6, 1657-1668.

Zaman, S., Lippman, S.I., Schneper, L., Slonim, N., & Broach, J.R. (2009). Glucose regulates transcription in yeast through a network of signaling pathways. *Molecular Systems Biology*, 5, 245.

Zaman, S., Lippman, S.I., Zhao, X., & Broach, J.R. (2008). How *Saccharomyces* responds to nutrients. *Annual Review in Genetics*, 42, 27-81.

Zuckerkandl, E., & Pauling, L. (1965). Evolutionary divergence and convergence in proteins. *Evolving Genes and Proteins*, 97, 97-166.

Zupancic, M.L., Frieman, M, Smith, D., Alvarez, R.A., Cummings, R.D., & Cormack, B.P. (2008). Glycan microarray analysis of Candida glabrata adhesin ligand specificity. *Molecular Microbiology*, 68, 547-559.

LIST OF PUBLICATIONS

Tzu Shan Ng, Mohd Nasir Mohd Desa, Doblin Sandai, Pei Pei Chong & Leslie Thian Lung Than. (2015). Phylogenetic and transcripts profiling of glucose sensing related genes in *Candida glabrata*. *Jundishapur Journal of Microbiology*. 8:e25177. doi: 10.5812/jjm.25177. (Journal Citation Reports 2015 Impact Factor: 0.655).

Tzu Shan Ng, Mohd Nasir Mohd Desa, Doblin Sandai, Pei Pei Chong & Leslie Thian Lung Than. (2016). Growth, biofilm formation, antifungal susceptibility and oxidative stress resistance of *Candida glabrata* are affected by different glucose concentrations. *Infection, Genetics and Evolution*. 40:331-338. doi: 10.1016/j.meedig.2015.09.004. (Journal Citation Reports 2015 Impact Factor: 2.591).

Tzu Shan Ng, Shu Yih Chew, Premmala Rangasamy, Mohd Nasir Mohd Desa, Doblin Sandai, Pei Pei Chong, Leslie Thian Lung Than. (2015). *SNF3* as high affinity glucose sensor and its function in supporting the viability of *Candida glabrata* under glucose-limited environment. *Frontiers in Microbiology*. 6:1334. doi: 10.3389/fmicb.2015.01334. (Journal Citation Reports 2015 Impact Factor: 4.165).

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